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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/768,781	01/25/2001	Gennady Merkulov	CL001057-CIP	3929

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CELERA GENOMICS CORP.
ATTN: WAYNE MONTGOMERY, VICE PRES, INTEL PROPERTY
45 WEST GUDE DRIVE
C2-4#20
ROCKVILLE, MD 20850

EXAMINER	
BASI, NIRMAL SINGH	

ART UNIT	PAPER NUMBER
1646	9

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/768,781	Merkulov et al
Examiner	**Art Unit**
Nirmal S. Basi	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 26, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *4, 8, 9, and 24-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *4, 8, 9, and 24-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Jan 25, 2001* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The Amendment filed 2/26/03 (paper number 8) has been entered.

2. Applicant's election of Group II (Claims 4-6, 8-11 and 22-23), cancellation of claims 1-3, 5-7, 10-23, addition of claims 24-29, amendment of claims 4 and 8, in Paper No. 6 (2/26/03) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is still deemed proper and is therefore made FINAL.

Objections

3. The drawings objected to because each Figure (ie Figures 1-3) must be labeled as Figure 1A, 1B etc, 2A, 2B etc. and 3A, 3B etc. and described separately in the Brief Description of the Drawings. The heading "DESCRIPTION OF THE FIGURE SHEETS" must be changed to Brief Description of the Drawings. Figures 1-3 must be described separately in the Brief Description of the Drawings as, e.g. Figure 1A-1x, Figure 2A-2x etc., where x is the last letter representing the set of Figures comprising the subsections of Figure 1, 2 or 3, or the equivalent, as required by 37 C.F.R. § 1.84 (u)(1). The Figures have not been labeled and described in correct format. The Figures are described as FIGURE 1, FIGURE 2 and FIGURE 3 in the specification and labeled as FIGURE 1, page 1 of 2, FIGURE 1, page 2 of 2 etc. in the drawings. Appropriate correction is required.

Also the SEQ ID Nos in the Figures do not correspond to the correct SEQ ID Nos in the

Sequence listing. Figure 1 discloses SEQ ID NO:4 to be a cDNA, Sequence listing discloses SEQ ID NO:4 to be protein. Figure 2 discloses SEQ ID NO:2 to be a protein, Sequence listing discloses SEQ ID NO:2 to be nucleic acid. Figure 3 discloses SEQ ID NO:4 to be a cDNA, Sequence listing discloses SEQ ID NO:4 to be protein. There are numerous errors in the specification when referring to the SEQ ID Nos. Of the nucleic acid and protein. For example, Page 18, third paragraph, discloses SEQ ID NO:2 is amino acid sequence, Sequence listing discloses SEQ ID NO:2 to be nucleic acid. Also, Page 18, third paragraph, disclose SEQ ID NO:4 is nucleic acid, Sequence listing discloses SEQ ID NO:4 to be protein. Applicant must check the entire specification to correct the numerous errors when referring to the SEQ ID NOs. The SEQ ID NOs. in the specification must correspond to the corresponding SEQ ID NO: in the Sequence listing. Appropriate correction is required.

4. ***Sequence Rules Compliance***

This application fails to comply with the sequence rules, 37 CFR 1.821-1.825. Nucleotide and polypeptide sequences must be identified with the corresponding SEQ ID NO. Title 37, Code of Federal Regulations, Section 1.821 states "reference must be made to the sequence by use of the assigned identifier", the identifier being SEQ ID NO. Sequences in Figures 2-3 must be identified by their corresponding SEQ ID NO:. Figure 2 contains many small peptide fragments that are not identified by SEQ ID NO:. Further, the "Query:33" and "Sbject:63" protein sequences, in Figure 2, must identified by their corresponding SEQ ID NO:. The sequences between the "Query:33" and "Sbject:63"sequence also must be identified by SEQ ID NO:. Also the DNA

disclosed in Figure 3, drawing pages 7-8 is not identified by SEQ ID NO:. Further, since Figure 3 contains two sequences it must be clarified which one of the sequences represents SEQ ID NO:3. Compliance with sequence rules is required.

Claim Rejection, 35 U.S.C. 112

5. Claims 4, 8-9, 24-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is indefinite because the nucleotide sequence cannot encode the polypeptide comprising the amino acid sequence of SEQ ID NO:2 because SEQ ID NO:2 is a polynucleotide sequence. Claim 4 is indefinite because the nucleotide sequence cannot consist of SEQ ID NO:3 because SEQ ID NO:3 is a amino acid sequence. Similarly, in claim 4, subsection (d), a nucleotide sequence cannot be completely complementary to an amino acid sequence.

Claim 26 is indefinite because the nucleotide sequence cannot consist of SEQ ID NO:3 because SEQ ID NO:3 is a amino acid sequence.

Claim 28 is indefinite because the nucleotide sequence cannot encode the polypeptide comprising the amino acid sequence of SEQ ID NO:2 because SEQ ID NO:2 is a polynucleotide sequence.

Claims 8-9, 24-25, 27 and are rejected for depending upon an indefinite base (or intermediate) claim and fail to resolve the issues raised above.

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 4, 8-9 and 24-29 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the invention. a "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. a "well established utility" is a utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. a "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention. Applicant has asserted utilities for the specifically claimed invention of claims 4, 8-9 and 24-

29. For example, the specification at page 1 asserts, the present invention provides peptides and proteins, including nucleic acid molecules encoding such peptides and protein molecules. The peptides and proteins of instant invention are claimed to be related to the XP transporter protein subfamily and they are stated to effect ligand transport. The relationship of claimed nucleic acid or its encoded polypeptide to XP proteins is not disclosed. Instant invention is claimed to be useful in the development of human therapeutics and diagnostic compositions and methods. Further, the specification discloses the nucleic acid molecules of present invention are useful for probes, primers, chemical intermediates, and in biological assays. The utilities disclosed in the specification are based on methods using claimed nucleic acid or the encoded polypeptide as a target for diagnosis and treatment in transporter-mediated and related disorders and for drug-screening methods using transporter peptides and polynucleotides to identify agonists and antagonists for diagnosis and treatment. The specification discloses transporter proteins regulate many different cell proliferation, differentiation and signaling pathways and mediate a wide variety of cellular functions. The claimed nucleic acid has been shown to be expressed in germinal center B cells and also in mixed tissue sample. The expression pattern of claimed nucleic acid does not provide a clear nexus to its function. The specification does not disclose which transporter protein is encoded by claimed nucleic acid, nor any disease states affected by its dysfunction. Further, the ligand affected or transported by the protein encoded by SEQ ID NO:1 is not disclosed. There is no clear showing that the polynucleotide of SEQ ID NO:1 encodes a XP protein. The specification fails to disclose the

relationship of the protein encoded by the polynucleotide of SEQ ID NO:1 to a particular transporter protein.

Neither the specification nor the art of record disclose the protein encoded by the polynucleotide of SEQ ID NO:1 is useful to identify drugs that affect said protein and modulate its activity. Similarly, neither the specification nor the art of record disclose any instances where disorders associated with claimed nucleic acid disfunction can be effected by interfering with the activity of the protein encoded by the polynucleotide of SEQ ID NO:1 or by interfering with polynucleotide of SEQ ID NO:. Thus the corresponding asserted utilities are essentially methods of treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed nucleic acid, vector comprising said nucleic acid or cells comprising said vector, further experimentation is necessary to attribute a utility to the claimed invention. See Brenner v. Manson, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

The specification discloses the nucleic acid of claimed invention encodes a transporter related to the XP protein subfamily, the subfamily or the specific degree of homology is not disclosed. The function is not disclosed. The ligand transported is not disclosed. Agonists and antagonists that may bind are not disclosed. Therefore based on the specification it can be concluded that the nucleic acid of present invention encodes a protein which may be a transporter protein, which in turn may be related to the some XP protein subfamily. The specification provides no data that the claimed nucleic acid expresses a functional transporter protein, its relationship to a particular XP subfamily, any ligands that activate, or the expression of claimed invention in a functional system that transports a particular ligand. Specific regions of the transporter protein required for activity are not disclosed.

Although the claimed polynucleotide of claimed invention is expressed in tissues there is no clear nexus between the expression of claimed polynucleotide and a disease state or dysfunction. There is no nexus relating methods of using the transporter protein/nucleic acid as a target for diagnosis and treatment in transport-mediated disorders. In light of the specification the skilled artisan can speculate that the claimed nucleic acid encodes a protein and may belong to the XP superfamily. However, no disclosure is provided within the instant specification on what specific function claimed transporter possesses, or how to specifically assay for such, ligands that bind, promoters that activate, nor are any disease states disclosed that are directly related to claimed invention dysfunction.

The specification discloses that the claimed polynucleotides are useful as tools for drug discovery, screening assays and the diagnosis of disease. For a utility to be "well-established" it must be specific, substantial and credible. All nucleic acids and genes and their encoded polypeptides may in some combination be useful in drug discovery, screening assays and the diagnosis of disease. However, the particulars of testing with SEQ ID NO:1-3 are not disclosed in the instant specification. The disease states, screening assays or ligands that bind to the protein encoded by claimed nucleic acid of instant invention are not identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO:1-3. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed polynucleotide in an array for screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicants' individual polynucleotide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polynucleotide has no "well-established" use. The artisan is required to perform further

experimentation on the claimed material itself in order to determine to what "use" any expression information regarding this nucleic acid could be put.

With regard to diagnosis of disease, in order for a polynucleotide or protein to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polynucleotide and a disease or disorder. The presence of a polynucleotide in a wide variety of tissue is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed cDNA or protein and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. The claimed polynucleotide is expressed in normal tissues and diseased tissues. Evidence of a differential expression might serve as a basis for use of the claimed polynucleotide as a diagnostic for a disease. However, in the absence of a clear disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

The specification fails to disclose sufficient properties of the protein and/or polynucleotide (SEQ ID NO:1-3) to support an inference of utility. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases and telomerases share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family.

Without some common biological activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity is known to be common to all members. To argue that all the members can be used for screening/testing for drugs, and diagnosis of disease, is to argue a general, nonspecific utility that would apply to virtually every member of the family, contrary to the evidence. Further, any compound could be considered as a regulator or modulator of tissue in that any compound, if administered in the proper amount, will stimulate or inhibit tissue. For example, salt, ethanol, and water are all compounds which will kill cells if administered in a great enough amount, and which would stimulate cells from which these compounds had been withheld, therefore, they could be considered regulators or modulators of

tissue. However, use of these compounds for the modulation of tissue would not be considered a specific and substantial utility unless there was some disclosure of, for example, a specific and particular combination of compound/composition and application of such in some particular environment of use.

Without knowing a biological significance of the claimed the polynucleotides or the polypeptide encoded thereby, one of ordinary skill in the art would not know how to use the claimed invention in its currently available form in a credible "real world" manner based on the diversity of biological activities possessed by transporter proteins. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

The utility of claimed transporter cannot be implicated solely from homology to known channels because the art does not provide teaching stating that all members of family must have the same effects, the same ligands and be involved in the same disease states. The claimed invention of instant invention is considered by the examiner to be possibly a member of the ion channel family. The art shows it requires more than the disclosed homology to assign a function to an orphan protein.

The specification asserts that the use of the claimed invention for drug discovery, screening assays and the diagnosis of disease are substantial utilities. The question at issue is whether or not the broad general assertion that the claimed nucleic acids might be used for *some* diagnostic application in the absence of a disclosure of *which* diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

Even though, instant invention may have some sequence homology to XK protein subfamily a reasonable correlation to its function and activity has not been established. The present rejection under § 101 follows *Brenner v. Manson*, as set forth above. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity,

and no disclosed common mode of action. Further a rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

Therefore, for reasons set forth above, the inventions of instant invention are rejected for lack of utility.

7. Claims 4, 8-9 and 24-29 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed nucleic acid, vector containing said nucleic acid, host cell comprising said vector, and method of producing polypeptide encoded by said nucleic acid, further experimentation is necessary to attribute a utility to the claimed nucleic acid molecule (polynucleotide consisting of SEQ ID NO:1) and its encoded protein.

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi NSB
Art Unit 1646
June 2, 2003

Michael D. Pak
MICHAEL PAK
PRIMARY EXAMINER